

DRUG THERAPY DURING PREGNANCY AND LACTATION





PREGNANCY

INTRODUCTION



Pregnancy and drug use:

- 8% of pregnant women's need drug treatment and more than 90% pregnant women's take prescription or non-prescription drugs.
- 59% of pregnant women's are prescribed other than vitamin or mineral supplements and 13% of pregnant women's are prescribed with dietary supplements.

Oxygen, Water , carbohydrates, lipids,
Electrolytes , Amino acids, vitamins,
Hormones, polypeptides, Viruses,
pathogens and Some drugs

Mother

P
L
A
C
E
N
T
A

carbon dioxide, water,
waste products, urea,
hormones

Fetus

INTRODUCTION



Placental drug transfer:

The drug is transferred through placenta by passive diffusion and **the factors that affecting placental transfer are,**

- protein binding
- pH difference
- Molecular weight
- Lipid solubility

Physiological changes during pregnancy :

- Wt gain and altered body shape
- Frequent urination
- Mouth and tooth changes
- Aches and pains
- Nausea and vomiting (morning sickness)
- Heart burns and leg cramps

INTRODUCTION



Pharmacokinetic changes in pregnancy:

- Increase plasma volume (30-50%)
- Increase cardiac output
- Increase renal blood flow and GFR
- Increase body fat
- Increase hepatic metabolism
- Increase progesterone levels
- Decrease plasma albumin concentration

INTRODUCTION



Drugs to be used during pregnancy :

Condition	Drugs used
Nausea & vomiting	Cyclizine, Meclizine, Metoclopramide (safe in 3 rd trimester of pregnancy)
Hypertension	Methyldopa
Cough	Diphenhydramine, Codeine, Dextromethorphan
Head ache	Paracetamol, codeine, Aspirin, Benzodiazepines & other NSAIDs (1 st & 2 nd trimester)
Anticoagulants	Heparin (S.C)
Anti- Amoebic drugs	Metoclopramide, Dilaxonide
Anti- migraine drugs	Ergometrine, Propranolol, Amitryptelline
Allergic Rhinitis	Glucocorticoids (locally), Diphenyl hydramine
Heart burns	Non-systemic antacids, Metoclopramide

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INTRODUCTION



Condition	Drugs used
Anti-diabetic drugs	Purified Insulin
Constipation	Milk of magnesia, Decussate sodium, Glycerin, Mineral oil, Bisacodyl
Peptic ulcer	Sucralfate, H ₂ blockers, non-systemic antacids, Bismuth sub- salicylates
Tuberculosis	Isoniazid, Ethambutol, Rifampin
Anti- asthmatics	Beta- agonists, Theophylline, Gluco-corticoids
Cardiac glycosides	Digoxin, Quinidine
Anti-malarial drugs	Cloroquine, Quinine
Anti-microbial drugs	Penicillin's, Cephalosporin's
Anti- helmintics	Piperazine, Biphenium

INTRODUCTION



ANTIBIOTICS CONTRAINDICATED DURING PREGNANCY :

DRUG	SIDE EFFECT
Metoclopramide Chloramphenicol Amino glycosides Tetracycline's	Hepatic failure Gray baby syndrome Ototoxicity Bone & teeth discoloration

TERATOGENESIS

TERATO – monster
GENESIS –producing

Teratogen is an infectious agent, drug, chemical/ radiant, that causes alterations in fetal morphology/ fetal functions when the fetus is exposed during critical stage of development.

Eg: 1. cleft lip/ palate, club foot, neural tube defects, missing/malformed limbs or fingers

2. Also behavioral and/ biochemical abnormalities

3. Teratogenesis is either direct i.e., malformation of structures or indirect, that interfering with Oxygen/ nutrients.



TERATOGENESIS



Malformation of drugs during pregnancy:

1. THALIDOMIDE:

This drug is 1st developed in Germany in 1954 by the pharmaceutical company i.e., chemie grunenthal.

- It is marketed in 1957 and spread to many countries like Europe, Asia, Australia, America & Africa.
- Thalidomide is used for insomnia, cold, cough, headache and morning sickness
- Used as anti-convulsive drug
- The 1st affected child birth are noticed in west Germany due to thalidomide on December 25, 1956. Later rare limb and ear defects are noticed & 40% of victims died before their 1st birthday.



because of this problems the thalidomide's are withdrawn from market by the end of November 1961.

TERATOGENESIS

Malformation of thalidomide:

phocomelia- it is derived from Greek word , in which

Phoco = seal

Melos = limbs

It indicates that the limb is like seal's flipper

- No ear/ deafness
- Missing / extra fingers & toes
- Partial/ total sight
- Improper formation of heart, brain and other internal organs
- Flattening of bridge of nose



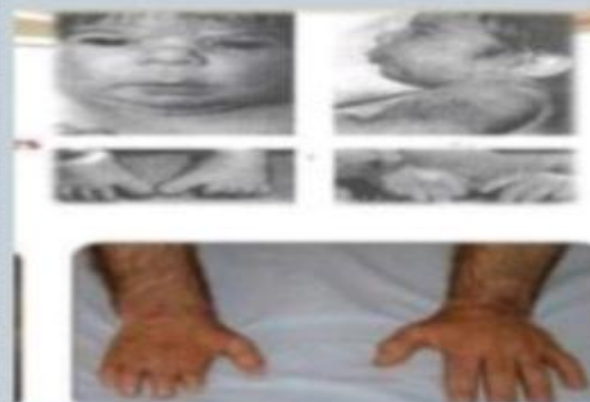
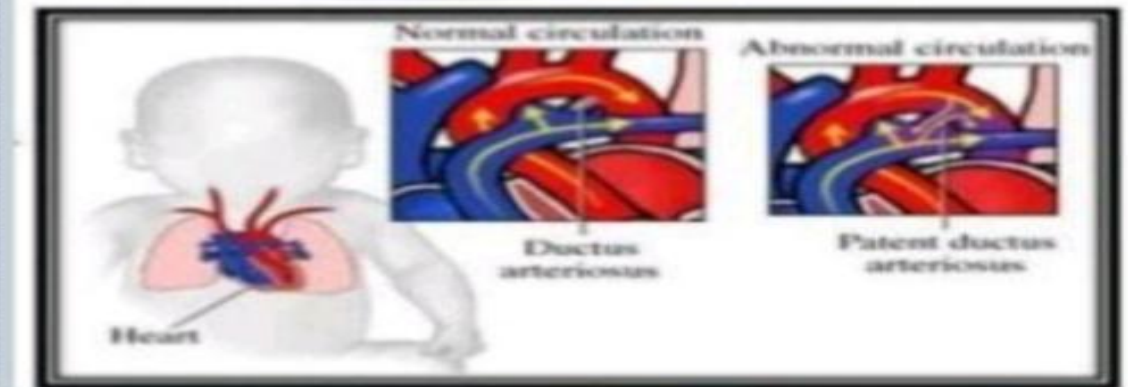
TERATOGENESIS

2. NSAIDs: if the NSAIDs are used 30 weeks on pregnancy onwards may causes,

- Premature closure of ductus arteriosus
- Oligohydramnios
- Deficiency of amniotic fluid

3. PHENYTOIN :

- Fetal hydantion syndrome
- Craniofacial abnormalities
- Hypo- plasia of distal phalanges
- Growth deficiency & mental deficiency
- Cleft Palate



Cleft palate, without cleft lip

TERATOGENESIS

4. VALPROIC ACID: it decreases absorption of folic acid & may causes neural tube defects.

5. CARBAMAZEPINE :

- Craniofacial abnormalities
- Spinal bifida
- Hypo- plasia of distal phalanges

6. PHENOBARBITOL:

- Neonatal withdrawal
- Neonatal coagulopathy

7. SULPHONAMIDES:

- Hyper bilirubinemia
- Jaundice
- Kernicterus



TERATOGENESIS

8. TRIMETHADIONE:

- Simian creases in the hands
- Cardiac anomalies
- Irregular teeth
- Mental retardation

9. DES (Diethyl stilbesterol):

- It increases risk of clear cell adenocarcinoma of vagina & cervix
- Breast cancer have been found in daughters of women who took DES during pregnancy
- Fertility problems in daughters of pregnant women's



TERATOGENESIS

10. WARFARIN:

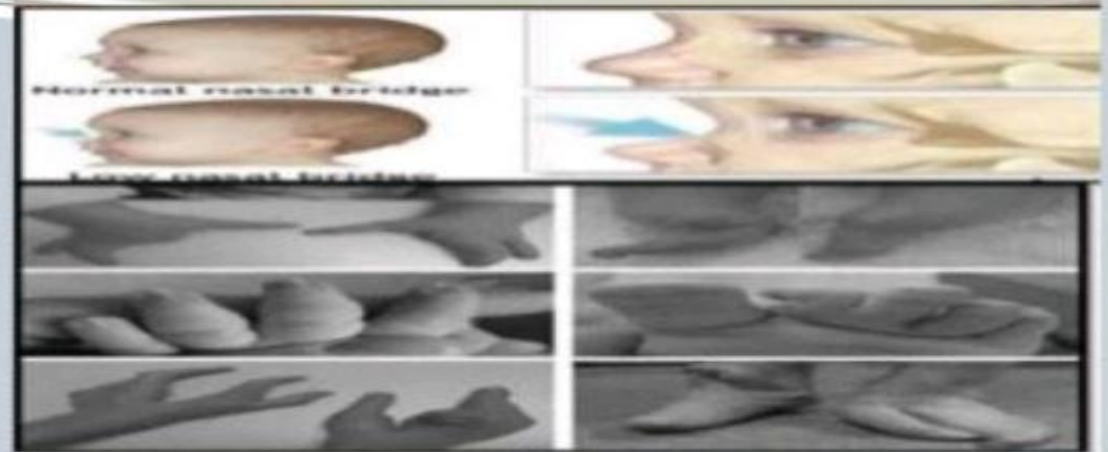
- Fetal warfarin syndrome
- Nasal hypo- plasia
- hypo- plasia of extremities
- Developmental retardation

11. COCAINE AND OPIODS :

- Neonatal abstinence syndrome
- Inadequate growth of fetus
- Premature birth defects

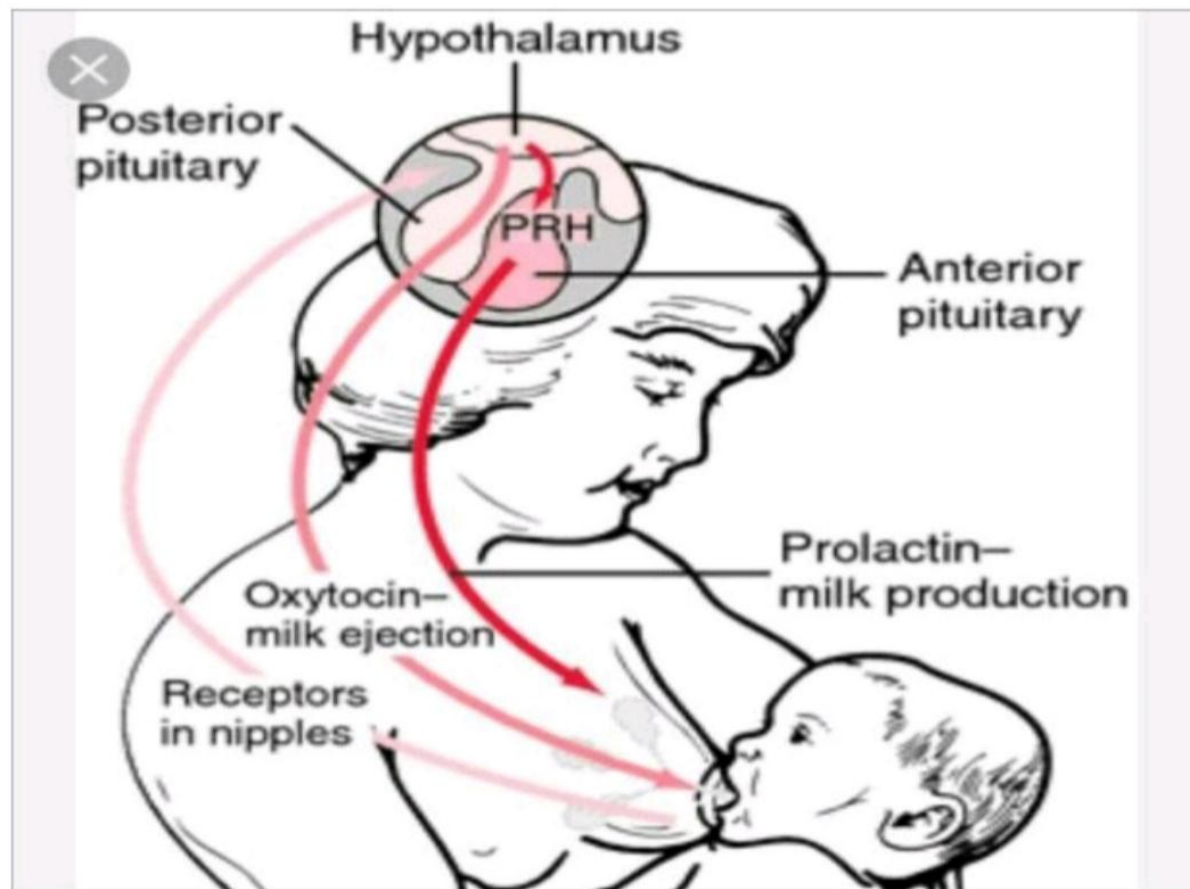
12. CIGARRATE SMOKING AND ALCOHOL CONSUMPTION :

- Birth defects in heart, brain and face
- Causes sudden infant death syndrome(SIDS)
- Premature labor and miscarriage
- Mental retardation





LACTATION



INTRODUCTION

This is the best way to delivered nutrients into infants, through the mother's milk the nutrients are transferred into children's.

DRUG PASSAGE INTO BREAST MILK:

The drug is passed into milk either by diffusion or active transport.

- Diffusion – movement of drug from high to low concentration
- Active transport – movement of drug from low to high concentration
- After diffusion or active transport, the drug is passes into breast milk through spaces between alveolar cells.



INTRODUCTION



DRUG TRANSFER INTO BREAST MILK:

- Ionization of drug – drugs which are non – protein bound non – ionized are more likely to be transferred into breast milk.
- Mol. Wt of drug – low mol. Wt drugs are more likely to be transferred into breast milk than high mol. Wt drugs.
- Solubility of drugs in lipids & water – lipid soluble drugs are easily soluble in breast milk than water soluble drugs.

DRUG CONCENTRATION IN BREAST MILK: The milk pH is lower than serum and variable in degree of fat concentration.

Changes in neonates:

- ✓ Vol. of milk consumed
- ✓ Higher gastric pH
- ✓ Difference in GI flora & GI transit time
- ✓ High concentration of drugs
- ✓ High % of body water
- ✓ Low metabolism & excretion rate

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Safe drugs in nursing mothers :

Category	Example
Anti – microbial drugs	Penicillin's & Cephalosporin's
Analgesics	Paracetamol, Morphine, Pentazocine
Anti – hypertensive's	Beta – blockers, Ca ²⁺ channel blockers
Anti – malarial drugs	Quinine, Chloroquine
Anti – tuberculotic's	Rifampin, Ethambutol, Pyrazinamide
Bronchodilators	Theophylline, Salbutamol
Anti – epileptic drugs	Phenobarbitone, Diphenyl hydantion, Valproic acid
Diuretics	Chlorthiazide, Furosemide, Spirano lactone
Hypoglycemic's	Insulin, Isoniazid, Tolbutamide

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Drugs to be avoided during lactation:

DRUG	EFFECT
Amiodarone	Neonatal hypothyroidism
Aspirin	Reye's syndrome
Barbiturate's	Drowsiness
Benzodiazepine's	Lathery
Cloramphenicol	Gray baby syndrome
Carbimazole	Hypothyroidism
Contraceptives	Dimish milk supply, decreases N2 & protein content
Tetracycline's	Tooth discoloration
Ephedrine	Irritability

INTRODUCTION

➤ **Drugs which are contraindicated in nursing mother's:**

Anti – cancer drugs, radio pharmaceuticals, ergot & it's derivatives, lithium, Thiouracil, Iodine, Mercurial's, sulphonamides, Atropine, chloramphenicol and phenyl butazone.

➤ **Drugs which suppress/inhibit Lactation:**

Bromocriptine, Bendro - flumethiazide, Estradiol, Oral contraceptive's, Levodopa, Trazodone.

➤ **Drugs which are hazardous to Infants :**

Large doses of Alcohol, Caffeine, Theophylline.

Considerations in breast feeding:

- ✓ With hold or delayed therapy if possible
- ✓ Use of drugs with poor penetration into milk
- ✓ Use an alternative route of administration
- ✓ Avoid nursing at peak concentration
- ✓ Pump & dump milk

